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**Proceedings Paper:**

Qvarnstrom, E.E. (2016) Regulation of Inflammatory and anti-apoptotic responses through the IL-1RI/TILRR complex. In: Biological Systems: Open Access. 4th International Conference on Integrative Biology, 18-20 Jul 2016, Berlin, Germany . OMICS International , p. 31.

<https://doi.org/10.4172/2329-6577.C1.005>

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## Regulation of inflammatory and anti-apoptotic responses through the IL-1RI/TILRR complex.

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Members of the toll-like and IL-1 receptor family (TIR) are central regulators of immune and inflammatory responses. Signal activation is induced through ligand binding and controlled by system specific co-receptors.

The IL-1RI co-receptor TILRR is a splice variant of FREM-1. TILRR association with the signalling receptor magnifies IL-1-induced activation of the canonical and non-canonical NF- $\kappa$ B network, by enhancing signal amplification at the level of the receptor complex and potentiate recruitment of the MyD88 adapter and PI3 kinase.

TILRR-controlled MyD88 dependent activation of the canonical pathway is regulated in a Ras-dependent manner, reflected in alterations in cytoskeletal structure and cell adhesion. The changes induced provide a process for rapid control of NF- $\kappa$ B, involving sequestration and release of cytoskeletal bound I $\kappa$ B $\alpha$  through a mechanism controlled by TILRR signal amplification. *In silico* simulations using agent based modelling of the NF- $\kappa$ B network predict cytoskeletal control of inhibitor levels to provide a mechanism for signal calibration, and to enable activation-sensitive regulation of NF- $\kappa$ B induced inflammatory responses.

Our studies have identified two functional sites within the TILRR core protein, which selectively control inflammatory and anti-apoptotic responses. The mechanisms underlying distinct network amplification, and the relevance of pathway-specific regulation of canonical and non-canonical NF- $\kappa$ B activation will be discussed.

### References

- Zhang, X., Shephard, F., Kim, HB., Palmer, IR., McHarg, S., Fowler, GJ., O'Neill, LA., Kiss-Toth, E., and Qwarnstrom, EE. *J Biol Chem.* 2010, 285: 7222-7232.
- Zhang, X., Montagut-Pino, G., Shephard, F., Kiss-Toth, E. and Qwarnstrom E E. *J. Biol. Chem.* 2012, 287: 12348-12352
- Rhodes, D., Smith S., Holcombe, M. and Qwarnstrom E.E. *PLoS One.* 2015, **10**: e0129888. doi: 10.1371/journal.pone.0129888.
- The studies were supported by UK government, BBSRC grants: BB/C515798/1, BBS/B/04056 and BB-J009687-1.